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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,341	04/23/2001	Adriano Aguzzi	30187/37275	2003

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EXAMINER	
CARLSON, KAREN C	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,341	AGUZZI ET AL.	
	Examin r	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10 and 13-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Invention I, Claims 1-9, 11, and 12 in is acknowledged. The traversal is on the ground(s) that Inventions I, IV, IX, and XII are sufficiently linked to form a single invention. This is not found persuasive because these are methods of using the factor that selectively interacts with PrP^{sc} and not with PrP^{c} and not the factor itself. Further, the elected factor does not appear to be allowable, and the methods will not be rejoined in accordance to *In re Ochiae* at this time.

The requirement is still deemed proper and is therefore made FINAL.

This application was filed April 23, 2001 and is a CIP of 09/407,667, filed September 28, 1999. The claimed invention is not found in prior US application 09/407,667.

Priority under 35 USC 119 is granted to PCT/EP01/03481, filed March 27, 2001. PCT/IB00/00849 was filed greater than one year prior to the instant application on June 26, 2000.

It is noted that many terms are specifically defined in the specification. At page 13, "**d rivative of plasminogen**" is specifically defined to be a peptide or protein which carries at least one amino acid addition, substitution, or deletion compared to the naturally occurring plasminogen or fragment thereof but still capable of selectively interacting with PrP^{sc} and not with PrP^{c}. Also on page 13, "**fragment of plasminogen**" is defined as a naturally occurring plasminogen which part is capable of selectively interacting with PrP^{sc} and not with PrP^{c}. The Examiner notes that plasminogen is well-known in the art, as are fragments and mutated forms of plasminogen well-known in the art – see cited art below, for example. Thus, one skilled in the art recognizes the structure of a derivative or a fragment of plasminogen as defined in the specification. The specification teaches plasminogen, fragments, and derivatives of plasminogen that selectively interacting with PrP^{sc} and not with PrP^{c}. Therefore, there is written

description for these plasminogen, fragments, and derivatives of plasminogen in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-9, 11, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, the term "factor" is so broad as to be vague, that is, is a factor any inorganic or organic chemical compound, peptide, or protein? What is the distinguishing structural feature of a factor? While this term is defined on page 12, it is exemplified and not specifically defined in terms of structure and of function. The term "interacts" is not clear – is the interaction electrostatic, binding, or just a molecular "bump"? Claims 11 and 12 refer to non-elected subject matter; therefore, the claims are indefinite for not particularly pointing out the elected subject matter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasminogen, fragments, and derivatives of plasminogen that selectively interacting with PrP^{sc} and not with PrP^{c}, does not reasonably provide enablement for any inorganic or organic chemical compound, peptide, or protein, for example, that may be encompassed by the term "factor", that selectively interact with PrP^{sc} and not with PrP^{c}. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary: The specification itself teaches that many serum proteins were tested to determine which serum proteins may bind to PrP^{sc} and not with PrP^{c}. Indeed, because there is a conformational difference in PrP^{sc} and PrP^{c}, different chemical environments were tested to determine if a factor selectively interacts with PrP^{sc} and not with PrP^{c}. Thus, it would require undue experimentation to determine other factor that will selectively interact with PrP^{sc} and not with PrP^{c}.

2) Amount of direction or guidance presented: With the quantity of experimentation used to arrive at the plasminogen, there is guidance.

3) Presence or absence of working examples: There are working examples.

4) Nature of the invention; 5) State of the prior art; 6) Relative skill of those in the art: The invention is complex and the prior art does not recognize other factors that selectively interact with PrP^{sc} and not with PrP^{c}. Those persons working in the art are highly skilled.

7) Predictability or unpredictability of the art: Given the volume of serum proteins tested, and experimental conditions tested, it is not predictable which factor will selectively interacting with PrP^{sc} and not with PrP^{c}.

8) Breadth of the claims: The claims are broad beyond the disclosure.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-9, 11, and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Fischer et al. (23 November 2000; Nature 408:479-483). Fischer et al. teach that plasminogen binds and interacts with PrP^{sc} and not with PrP^{c} (page 479, right col., para. 1 and Fig. 3; Claim 1, 5-7). Fragments and derivatives of plasminogen comprising kringle domains I-III or LBS-1 also bound to PrP^{sc} and not with PrP^{c} (page 482, left col., para. 3 and Fig. 4c; Claims 1, 2). The interaction of plasminogen with PrP^{sc} was at the C-terminal of PrP^{sc} (page 482, right col., top; Claim 3). At page 481, right col., Fischer et al. demonstrates that plasminogen binds to PrP^{sc} from human or from mouse (Claim 4). Plasminogen, kringle I-III, and LBS-1 bound or not bound to PrP^{sc} were placed on carriers (Claim 8) such as paramagnetic beads (page 479, right col., para. 1 and Methods), beads, sandwich binding assay (liquid carrier undergoing phase transition to solids), and western blots which also comprise filter strips. While not specifically mentioned, western blots and binding assays are generally carried out in microtiter plates or microarray plates. Thus, Claim 9 is anticipated. At page 482, right col. and Methods, the plasinogen was placed into PBS and therefore a pharmacological solution (Claim 12). The diagnostic kit of Claim 11 is not defined over the teachings of Fischer et al. (Claim 11).

Claims 1-4, 8, 9, 11, and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Folkman et al. (USP 6,521,439, priority to March 8, 1996). Folkman et al. teach plasminogen and plasminogen fragments, especially kringle domains I-III which the specification teaches binds to PrP^{sc} and not with PrP^{c}, at the C-terminus of PrP^{sc}, of a variety of species (Claims 1-4). The plasminogen and fragments were placed into a carrier (Claim 8) and placed on SDS-PAGE (Examples 15, 16, for example; Claim 9) The diagnostic kit of Claim 11 is not defined over the teachings of Folkman et al. and Folkman et al. teach kits at col. 26 (Claim 11). Plaminogen and plasminogen fragments were placed into a pharmaceutical composition and administered to mice (Example 17, for example; Claim 12).

Claims 1-4, 8, 9, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Silverstein et al. (USP 3,943,245; issued March 9, 1976). Silverstein et al. teach the purification of plasminogen, which the specification teaches binds to PrP^{sc} and not with PrP^{c}, at the C-terminus of PrP^{sc}, of a variety of species (Claims 1-4). Plasminogen was placed into a carrier and onto a Sepharose L-lysine columns (Claim 8, 9)). Plasminogen was placed into PBS (Example IV), and therefore a pharmaceutical composition (Claim 12). The diagnostic kit of Claim 11 is not defined over the teachings of Silverstein et al. (Claim 11).

Claims 1-4, 8, 9, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Dawson et al. (USP 5, 688,664, issued November 18, 1997). Dawson et al. teach plasminogen having a variety of mutations; thus, Dawson et al. teach derivatives of plasminogen. These mutations are not in the kringle domains I-III and thus should not affect binding to PrP^{sc} (Claim 1-4). The diagnostic kit of Claim 11 is not defined over the teachings of Dawson et al. (Claim 11). The mutated plasminogens were placed in ApTT reagent, and therefore a carrier (Claim 8, and

placed into microtitre plates (see Example 11, 2.2; Claim 9.The mutated plamsinogens were placed in a buffer, and thus a pharmaceutical composition (Example 11, 2.1; Claim 9).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 703-308-0034. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 703-308-2329. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

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KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER